

### **AMENDMENTS TO THE CLAIMS:**

Please amend claims 13, 14, 32, 34, 36, 37, 40 and 42 as follows. Please cancel claims 16 and 41 without prejudice or disclaimer, and add claims 45-51. This listing of claims replaces all prior versions, and listings of claims, in the application.

### **LISTING OF CLAIMS:**

1. (Previously Cancelled)
2. (Previously Amended) The targeted vector delivery particle of claim 32, wherein the targeting agent or portion thereof that triggers phosphatidylinositol-3-OH kinase (PI3K) activation is selected from the group consisting of proteins that bind to G-protein coupled receptors.
3. (Previously Amended) The targeted delivery vector particle of claim 32, wherein the bifunctional molecule comprises a linker that links the antibody or antigen-binding portion thereof to the targeting agent.
4. (Previously Amended) The targeted delivery vector particle of claim 32, wherein the bifunctional molecule comprises a fusion protein.
5. (Previously Amended) The targeted delivery vector particle of claim 32, wherein the bifunctional molecule comprises chemically conjugated polypeptides.
6. (Previously Amended) The targeted delivery vector particle of claim 3, wherein the linker is a single amino acid or a peptide.
7. (Previously Amended) The targeted delivery vector particle of claim 32, wherein the antibody comprises a heavy chain or a portion thereof sufficient for antigen-binding fused to the targeting agent.
8. (Previously Amended) The targeted delivery vector particle of claim 32, wherein the antibody portion is an Fab'2 fragment.
9. (Previously Amended) The targeted delivery vector particle of claim 32, wherein the antibody portion comprises a sufficient portion of the variable regions of the heavy and light chains for antigen recognition.
10. (Previously Amended) The targeted delivery vector particle of claim 32, wherein the antibody comprises the sequence of amino acids set forth in SEQ ID No. 2 or SEQ ID No. 6 or a sufficient portion thereof for antigen recognition.
11. (Previously Amended) The targeted delivery vector particle of claim 32, wherein the antibody comprises the sequence of amino acids set forth in SEQ ID No. 4 or a sufficient portion thereof for antigen recognition.

12. (Previously Amended) The targeted delivery vector particle of claim 32, wherein the antibody portion is an Fab fragment.

13. (Currently Amended) The targeted delivery vector particle of claim ~~40~~ 32, wherein the antibody portion ~~of the vector particle is encoded by a sequence of nucleic acids that~~ includes a sequence of ~~nucleic acids~~ amino acid selected from among:

(a) ~~the coding portion of the sequence of nucleotides~~ amino acids set forth in SEQ ID No. ~~[[1 ] 2~~ or SEQ ID No. ~~[[5]] 6~~ or a sufficient portion thereof for antigen recognition;

~~(b) a sequence of nucleotides that comprises one or more degenerate codons of (a);~~  
and

~~[[c]]~~ b) a sequence of amino acids encoded by a sequence of nucleotides that hybridizes along its full length under conditions of high stringency to a sufficient portion of the coding portion of the sequences of nucleotides set forth in SEQ ID No. 1 or SEQ ID No. 5 ~~(a) or (b)~~ to encode an antigen-binding portion of the antibody.

14. (Currently Amended) The targeted delivery vector particle of claim ~~41-32~~, wherein the antibody portion ~~of the vector particle is encoded by a sequence of nucleic acids that~~ includes a sequence of ~~nucleic acids~~ amino acids selected from among:

(a) ~~the coding portion of the sequence of nucleotides~~ amino acids set forth in SEQ ID No. ~~[[3 ] 4~~ or a sufficient portion thereof for antigen recognition;

~~(b) a sequence of nucleotides that comprises one or more degenerate codons of (a);~~  
and

~~[[c]]~~ b) a sequence of amino acids encoded by a sequence of nucleotides that hybridizes along its full length under conditions of high stringency to a sufficient portion of the coding portion of the sequences of nucleotides set forth in SEQ ID No. 3 ~~(a) or (b)~~ to encode an antigen-binding portion of the antibody.

15. (Previously Amended) The targeted delivery vector particle of claim 32, wherein the bifunctional molecule comprises the sequence of amino acids set forth in any of SEQ ID Nos. 7-14 for specific binding to a targeted receptor.

16. (Cancelled)

17. (Previously Cancelled)

18. (Previously Amended) The targeted delivery vector particle of claim 32, wherein the antibody or portion thereof specifically binds to the penton base or penton fiber or the complex thereof of an adenovirus.

19. (Previously Amended) The targeted delivery vector particle of claim 32, wherein the antibody or portion thereof specifically binds to an antigen that includes an RGD motif.

20. (Previously Amended) The targeted delivery vector particle of claim 32, wherein the targeting agent comprises all or sufficient portion thereof of a protein that binds to G-protein coupled receptors, oncogene product receptors, hormone receptors or cytokine receptors that employ the PI3 signaling pathway for signal transduction,

wherein the sufficient portion thereof specifically binds to the cell surface receptor therefor and internalizes linked viral particles.

21. (Previously Amended) The targeted delivery vector particle of claim 32, wherein the targeting agent comprises all or sufficient portion thereof of a protein that binds to G-protein coupled receptors that employ the PI3 signaling pathway for signal transduction,

wherein the sufficient portion thereof specifically binds to the cell surface receptor therefor and internalizes linked viral particles.

22. (Previously Amended) The targeted delivery vector particle of claim 32, wherein the targeting agent comprises all or sufficient portion thereof of hormone or growth factor or cytokine,

wherein the sufficient portion thereof specifically binds to the cell surface receptor therefor and internalizes linked viral particles.

23. (Previously Amended) The targeted delivery vector particle of claim 6, wherein the targeting agent or portion thereof is a tumor necrosis factor (TNF), a fibroblast growth factor (FGF), an insulin-like growth factor (IGF), a colony stimulating factor (CSF), insulin or a stem cell factor (SCF).

24. (Previously Amended) The targeted delivery vector particle of claim 6, wherein the targeting agent or portion thereof is insulin, insulin-like growth factor-1 (IGF-1), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), stem cell factor (SCF), colony stimulating factor (CSF), a platelet-derived growth factor (PDGF), a fibroblast growth factor (FGF), a heparin binding epidermal growth factor (HBEGF), a vascular endothelial growth factor (VEGF) or dimer thereof.

25. (Previously Amended) The targeted delivery vector particle of claim 6, wherein the targeting agent or portion thereof is tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), insulin-like growth factor-1 (IGF-1), stem cell factor (SCF) or an epidermal growth factor (EGF).

26. (Previously Amended) The targeted delivery vector particle of claim 32, wherein the targeted cell surface protein is selected from among a PDGF receptor, an IGF-1

receptor, an EGF receptor, a member of the FGF receptor family, a TNF receptor, a CSF-1 receptor, an insulin receptor, an IGF-1 receptor, an NGF receptor, an IL-2 receptor, an IL-3 receptor, an IL-4 receptor, an IgM receptor, a CD4 receptor, a CD2 receptor, a CD3/T cell receptor, a G protein linked thrombin receptor, an ATP receptor, and an fMLP receptor.

27. (Previously Amended) The targeted delivery vector particle of claim 32, wherein the targeted cell surface protein is selected from among tyrosine kinase receptors that, when activated, result in increased accumulation of PtdIns(3,4,5)P3, and receptors associated with the src family non-receptor tyrosine kinases that stimulate PI3Ks to lead to PtdIns(3,4,5)P3 accumulation.

28. (Previously Cancelled)

29. (Previously Cancelled)

30. (Previously Amended) The targeted delivery vector particle of claim 32, wherein the vector genome encodes a therapeutic product.

31. (Previously Cancelled)

32. (Currently Amended) A targeted delivery vector particle, comprising:

(a) a fiberless adenovirus particle;

(b) a bifunctional molecule, comprising an antibody or antigen-binding portion thereof and a targeting agent, wherein:

the antibody or antigen-binding portion specifically binds to penton ~~an antigen in a protein on the particle; the protein on the particle binds to~~ on the particle, whereby the bifunctional molecule is linked to the particle and interaction of the particle with  $\alpha_v$  integrin is bypassed; and

the targeting agent specifically binds to a cell surface protein that activates the phosphatidylinositol 3 (PI3) signaling pathway; and

(c) a fiberless adenovirus vector genome in the particle.

33. (Cancelled)

34. (Currently Amended) The targeted delivery vector particle of claim 32, wherein the antibody portion of the bifunctional molecule is covalently linked to a ~~viral particle surface protein~~ penton or a component thereof.

35. (Previously Cancelled)

36. (Currently Amended) A combination, comprising:

a fiberless adenoviral vector particle for delivering gene products to targeted cells; and

a bifunctional molecule that comprises:

an antibody or antigen-binding portion and a targeting agent, wherein:

the antibody or antigen-binding portion specifically binds to penton, whereby interaction with  $\alpha_v$  integrin of an adenovirus particle displaying the bifunctional molecule is bypassed to an antigen in a protein on a viral particle that binds to  $\alpha_v$  integrin; and

the targeting agent specifically binds to a cell surface protein that activates the phosphatidylinositol 3 (PI3) signaling pathway.

37. (Currently Amended) The combination of claim 36, wherein:  
the bifunctional molecule and ~~delivery~~ vector particle for delivering gene products to targeted cells are complexed via penton in the vector particle.

38. (Previously Cancelled)

39. (Previously Cancelled)

40. (Currently Amended) A fiberless adenoviral particle, comprising a bifunctional molecule ~~of claim 10~~ that contains an antibody or antigen-binding portion and a targeting agent, wherein:

the antibody or antigen-binding portion interacts with penton to display the bifunctional molecule on the particle, whereby interaction of the particle with  $\alpha_v$  integrin is bypassed; and

the targeting agent specifically binds to a cell surface protein that activates the phosphatidylinositol 3 (PI3) signaling pathway.

41. (Cancelled)

42. (Currently Amended) A bifunctional molecule, comprising:  
an antibody or antigen-binding portion and a targeting agent, wherein:  
the antibody or antigen-binding portion comprises all or a portion of DAV-1 antibody, wherein the portion thereof binds to a component of penton, whereby upon binding of the antibody portion to penton, interaction of penton with  $\alpha_v$  integrin is inhibited; and

the targeting agent specifically binds to a cell surface protein that activates the phosphatidylinositol 3 (PI3) signaling pathway.

43. (Previously Presented) A fiberless adenoviral particle, comprising a bifunctional molecule of claim 42.

44. (Previously Presented) The combination of claim 36 that is packaged as a kit, optionally containing instructions for use thereof.

45. (Previously Presented) The targeted delivery vector particle of claim 10, wherein the antibody portion is an Fab fragment.

46. (New) An adenoviral particle, comprising a bifunctional molecule that contains an antibody or antigen-binding portion and a targeting agent, wherein:

the antibody or antigen-binding portion interacts with penton to display the bifunctional molecule on the particle, whereby interaction of the particle with  $\alpha_v$  integrin is bypassed; and

the targeting agent specifically binds to a cell surface protein that activates the phosphatidylinositol 3 (PI3) signaling pathway.

47. (New) The targeted delivery vector particle of claim 46, wherein the antibody or portion thereof specifically binds to an RGD motif in penton.

48. (New) The targeted delivery vector particle of claim 46, wherein the targeting agent comprises all or sufficient portion thereof of a protein that binds to G-protein coupled receptors, oncogene product receptors, hormone receptors or cytokine receptors that employ the PI3 signaling pathway for signal transduction,

wherein the sufficient portion thereof specifically binds to the cell surface receptor therefor for activation of the PI3 signaling pathway.

49. (New) The targeted delivery vector particle of claim 47, wherein the antibody is DAV-1 or a portion thereof.

50. (New) The targeted delivery vector particle of claim 46, wherein the targeted cell surface protein is selected from among a PDGF receptor, an IGF-1 receptor, an EGF receptor, a member of the FGF receptor family, a TNF receptor, a CSF 1 receptor, an insulin receptor, an IGF 1 receptor, an NGF receptor, an IL-2 receptor, an IL-3 receptor, an IL-4 receptor, an IgM receptor, a CD4 receptor, a CD2 receptor, a CD3/T cell receptor, a G protein linked thrombin receptor, an ATP receptor, and an fMLP receptor.

51. (New) The targeted delivery vector particle of claim 46, wherein the antibody or portion thereof specifically binds to the penton base of an adenovirus particle.